NSCLC patients with known targetable molecular mutations is treatment of limited metastatic progression or *oligoprogression*. This is due to the fact that most patients with treatable mutations in NSCLC progress in a limited number of metastases. Ablation of these metastases has been shown to allow patients to remain on therapy longer thereby extending the time to the next line of therapy.
Melanoma and Renal Cell Carcinoma, classically described "radioresistant" histologies, respond well to ablative radiation. Ablation of all known metastases has resulted in high (80-90%) rates of treated tumor control. Comparative analyses of metastastic melanoma patients treated with metastasectomy versus standard of care demonstrated improved survival for those treated with removal of metastases. However this was prior to the advent of improved immunomodulatory and targeted agents for metastatic melanoma. Furthermore, treatment of oligometastases with radiation has the potential to act as an immunosensitizer, stimulating the immune system and enhancing the response to immunomodulatory agents, perhaps inducing an abscopal effect.
Evidence also shows that oligometastases are common in prostate cancer. Ongoing studies are determining if ablative therapy to all known prostate oligometastases can delay the onset of androgen deprivation therapy, limiting the time, side effects and cost associated with treatment.
There are other roles for treatment of oligometastases beyond improvements in survival vs standard therapies. Many patients are not candidates for standard therapies due to medical comorbidity. Other patients, intolerant of the side effects of "targeted therapies", are left with few treatment options. Ablation of all metastases through surgery if feasible and possible or radiation can serve as another line of therapy to prolong disease free intervals.

SP-0497
Controversies and clinical trials in oligometastatic disease
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Although the term 'oligometastasis' was coined in the 1990's, the first reports of treating limited metastatic disease with surgical resection originated six decades earlier. Several modalities are available to treat metastatic lesions, including surgical resection, stereotactic radiotherapy, conventional radiotherapy, and radiofrequency ablation.
Numerous studies have reported 'better than expected' survival outcomes after ablation of limited metastatic disease, encompassing patients with varied histologic subtypes and metastatic locations. However, significant controversies remain, as it is unclear as to the extent of which the 'better than expected' survival is due to the treatments themselves, or merely due to selection of very fit patients with indolent-behaving tumors. The goal of this presentation is to review the uncertainties associated with the oligometastatic state, the natural history of untreated oligometastatic disease, current and past clinical trials, and future areas of research.

Symposium with Proffered Papers: Immunotherapy and radiotherapy

SP-0498
Ablative radiation-mediated tumour control depends on DNA sensing and T cell responses
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It is thought that ablative radiotherapy (RT), used for rapid control tumor growth, induces genotoxic stress and mitosis crisis leading to prolonged dormancy of irradiated tumor at local and distal site in most patients. We have unexpectedly observed that initial reduction of tumor burden following ablative RT also depends largely on type I IFN for CTL. Targeting tumor with IFN can control tumor growth through initiating a coordinated innate and adaptive immune attack against tumor cells. However, the mechanism for radiation-mediated type I IFN induction remains unclear. Here, we demonstrated that STING, but not MYD88, was required for type I IFN-dependent antitumor effects of radiation. STING in dendritic cells (DCs) controlled radiation-mediated IFN-β induction and was activated by irradiated-tumor cells. The cytosolic DNA sensor cyclic GMP-AMP synthase (cGAS) mediated DCs sensing of irradiated-tumor cells. Moreover, STING was essential for radiation-induced adaptive immune responses, which relied on type I IFN signaling on DCs. Exogenous IFN-β treatment rescued cGAS/STING-deficient immune responses. Accordingly, enhancing STING signaling by cGAMP administration promoted antitumor efficacy of radiation. Our results reveal that the molecular mechanism of radiation-mediated antitumor immunity depends on a proper cytosolic DNA-sensing pathway, pointing towards a new understanding of radiation and host interactions. Furthermore, we uncover a new strategy to improve radiotherapy by cGAMP treatment. RT induced IFN can also upregulate PD-L1 that suppress T cell-mediated damage and develop radiation resistance for relapse over time. Anti-PDL-1 antibody can greatly reduce radiation resistance leading to complete tumor regression. Furthermore, our study challenges the rationale for current radio/chemotherapy strategies and highlights the importance of immune activation in preventing tumor relapse.

SP-0499
Understanding biological pathways mediating response to radioimmunotherapy
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Cells respond to radiation. The best known pathways involve DNA repair and anti-apoptotic activities. These have different effects on the cell, its environment and the resulting immune response. We will discuss a new mechanism of DNA repair control that makes cells less responsive to radiation and DNA damaging chemotherapies. In addition, local radiotherapy can boost antibody-based triggering of immune responses to tumors but also makes the cells and environment more susceptible for CTL based therapies. This has allowed us to perform genome-wide screens to identify new and unknown factors controlling DNA repair and susceptibility to DNA damaging regimes in cancer therapy. We will discuss how